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Anesthesia and neuromuscular block management in thymectomies performed in cases of thymoma and myasthenia gravis: A retrospective study

Anesthesia management in thymectomies performed in myasthenia gravis

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Abstract

Aim: The aim of our study was to evaluate anesthesia management and the antagonism of neuromuscular blockade with sugammadex in thymectomies performed in patients with thymoma and myasthenia gravis (MG), especially in terms of the postoperative residual block, complications, and its effect on postoperative respiratory pattern.

Material and Methods: In order to evaluate the effectiveness of the anesthesia methods and neuromuscular block management procedures we use in thymectomy cases in our clinic, patient files, anesthesia record forms, early postoperative follow-up, and the discharge process were retrospectively reviewed. Patients who underwent thymectomy, used steroid neuromuscular blocking agents (NMBA) and preferred sugammadex for neuromuscular block antagonism were included in the study.

Results: There was no difference between the time of anesthesia and surgery in patients, the total doses of rocuronium and sugammadex used, the time between the onset of spontaneous respiration and extubation, and the time when spontaneous respiration was started without any intervention. In the early postoperative period, complications such as reintubation due to respiratory failure, a decrease in peripheral O2 saturation below 90%, postoperative residual neuromuscular block were not observed.

Discussion: We recommend using propofol as an intravenous general anesthetic agent in thymectomy surgery applied to patients with MG, performing total intravenous anesthesia using propofol and opioid analgesics in anesthesia maintenance, and providing a good peroperative analgesia control. In addition, we think that sugammadex may be preferred for steroid NMBA antagonism in this patient group.

Keywords

Thymoma; Myasthenia gravis; Anesthesia; Neuromuscular block; Sugammadex

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Introduction

Myasthenia gravis (MG) is a neuromuscular autoimmune disease caused by the development of antibodies against nicotinic acetylcholine receptors. The main pathology is the reduction of nicotinic acetylcholine receptors (nAChR) at the neuromuscular junction.

Thymoma occurs in 10% to 15% of patients affected by MG [1]. Thymoma is a benign thymus tumor that produces mostly acetylcholine receptor autoantibodies and sometimes autoantibodies against certain muscle proteins such as the titin and ryanodine receptor [2].

In addition to pharmacological treatment, thymectomy is a standard treatment for MG, but anesthesia management and application are characteristic according to the type of surgery to be performed. Patients with MG are highly sensitive to nondepolarizing neuromuscular blocking agents (NMBA). At the same time, resistance to the depolarizing NMBA may develop. In these patients, as important as preoperative evaluation and intraoperative case management, it is as important in postoperative recovery and follow-up. Since these patients may develop residual neuromuscular block, postoperative respiratory failure risk and related complications due to the use of NMBA. Postoperative residual block may cause aspiration and life-threatening respiratory failure. Insufficient muscle strength can cause hypoventilation, oxygen desaturation, the development of hypercapnia, micro-and macro aspirations, and postoperative bronchopneumonia in the postoperative period [3].

Sugammadex is the first selective binding agent containing eight glucose molecules in a gamma-cyclodextrin structure that reverses the effect of steroid NMBA. Sugammadex reduces its activity by encapsulating steroidal NMBA such as rocuronium and vecuronium. Unlike anticholinesterase, sugammadex does not increase acetylcholine in neuromuscular connections and does not interfere with the perioperative anticholinesterase level. Therefore, sugammadex may be an ideal drug for the reversal of muscle paralysis in MG patients [4-6].

In this study, anesthesia-neuromuscular block management and neuromuscular block antagonism using sugammadex were investigated in thymectomy cases in thymoma and MG patients. The aim of our study was to evaluate anesthesia management in thymectomies performed in patients with thymoma and MG, to evaluate the antagonism of neuromuscular block with sugammadex, postoperative residual block, complications, and its effect on the postoperative respiratory pattern, and to confirm whether sugammadex can provide complete and rapid recovery of neuromuscular block in MG patients.

Material and Methods

For this study, permission was obtained from the local ethics committee with protocol number 2020/375. This work covers 30 cases over the age of 18 who underwent thymectomy surgery performed in patients with thymoma and MG between the years 2015-2020. While 15 of the cases were to be operated on due to thymoma only, 15 of them were patients who were treated with a diagnosis of MG, were diagnosed with thymoma, and were scheduled for thymectomy. Anesthesia management and neuromuscular block antagonism using sugammadex were examined in thymectomy surgery applied to these patients (Figure 1).

In order to evaluate the effectiveness of the anesthesia methods and neuromuscular block management procedures we use in thymectomy cases in our clinic, patient files, anesthesia record forms, early postoperative follow-up, and discharge process were retrospectively reviewed. Patients who underwent thymectomy, older than 18 years of age, used steroid NMBA and preferred sugammadex for NMB antagonism were included in the study.

Demographic data of the patients, American Society of Anesthesiologists (ASA) risk scores, postoperative intensive care unit (ICU) process, duration of stay in the ICU, duration of anesthesia-surgery, time to start spontaneous and unsupported breathing, surgical treatment method, drugs, and doses were scanned from records. All patients are followed up in the ICU for at least 24 hours in terms of postoperative residual block or other complications.

Anesthesia Application and Neuromuscular Block Management: In our hospital, the same monitoring and anesthesia practices are performed as the anesthesia protocol in thymectomy surgery. In this direction, in all patients, electrocardiography, non-invasive blood pressure measurement, peripheral oxygen saturation (SpO_2), end-tidal carbon dioxide pressure ($EtCO_2$), neuromuscular function monitoring, invasive arterial pressure, temperature monitoring and Bispectral Index (BIS) monitoring are performed. The targeted BIS value is between 40-60 in all cases.

As a routine anesthesia procedure, propofol (2--2.5 mg/kg), fentanyl (1 μg/kg) are used in anesthesia induction, and anesthesia maintenance is provided by propofol and remifentanil infusion in a 40% O_2- 60% air mixture. Deep NMB is targeted in all patients for patient comfort and ease of operation. Nerve muscle activity monitorization is performed by the adductor pollicis muscle with the acceleromyography method (TOF-Watch® SX, Shering Plough Dublin Ireland). Rocuronium is used at a dose of 0.6 mg/kg in all patients. When the train-of-four (TOF) value is zero, endotracheal intubation is performed. The neuromuscular block is achieved with a TOF 2 ≤ by administering additional rocuronium (0.15 mg / kg) when necessary. When the surgical procedure is completely finished, sugammadex is administered at a dose of 2 mg / kg. When the TOF ratio is ≥0.9, the TOF measurement is terminated and the patients are extubated. The time elapsed starting from spontaneous breathing until extubation, and the time from the end of the surgery until unaided breathing become sufficient without the need for airway maneuver and ventilation were examined. Patients who are awake, oriented, clinically strong enough, and have an Aldrete score of ≥9 are taken into the intensive care unit and followed up for at least 24 hours.

Statistical Analysis

The data were analyzed using the Statistical Package for Social Sciences (SPSS Inc., Chicago, IL) Version 23.0. The normal distribution of numerical variables was evaluated with the Kolmogorov-Smirnov test. Descriptive statistics were made. Numerical variables were given as mean ± standard deviation (SD) and median (IQR: 25% -75%,) and categorical variables as number (n) and percentage (%).The level of statistical significance was taken as $p < 0.05$.

Results

Among our demographic findings, 30 patients whose records were fully reached were included in the study. While 15 of the cases were to be operated on due to thymoma only, 15 of them were patients who were treated with a diagnosis of MG, were diagnosed with thymoma, and were scheduled for thymectomy. While our patient population showed homogeneity in terms of age, body weight, duration of anesthesia-surgery, total rocuronium, and sugammadex dose used, it was heterogeneous in terms of MG classification and characteristics of patients with MG (Tables 1, 2).

Intravenous general anesthesia was used as an anesthesia method in surgical procedures. While the thoracic epidural catheter was inserted in 26 (86.7%) of our patients for postoperative analgesia, the procedure was unsuccessful in 4 patients.

For NMB, rocuronium was administered at a dose of 0.6 mg/kg in all patients. In patients undergoing neuromuscular block monitoring, additional rocuronium (0.15 mg/kg) was administered when necessary, with a TOF $\leq$ 2. Sugammadex at a dose of 2 mg/kg was used for NMB antagonism. Additional doses of sugammadex were not needed.

There was no difference between the times of anesthesia and surgery in patients, the total doses of rocuronium and sugammadex used, the time between the onset of spontaneous respiration and extubation, and the time when spontaneous respiration was started without any intervention are shown in Table 2.

Table 1. Demographic Findings and Characteristics of patients with Myasthenia Gravis

	n=30 (%)
Age [years, (mean±SD)]	45.27±15.31
Gender [female/ male, n (%)]	17/13(43.3/56.7)
Body mass index (kg/m2)	25.47±2.67
ASA [2/3, n (%)]	19/11(63.3/36.7)
Osserman Classification in Myasthenia Gravis	n=15 (%)
I only ocular involvement	2 (13.4)
IIa Mild generalized weakness	6 (40.0)
Ib Moderate generalized weakness, bulbar dysfunction, or both	7 (46.6)
Comorbid Diseases in Patients with Myasthenia Gravis	n=15 (%)
Hypertension	7 (46.6)
Diabetes Mellitus	1 (6.6)
Thyroid Dysfunction	4 (26.6)
Asthma Bronchiale	4 (26.6)
Clinical Findings in Patients with Myasthenia Gravis	n=15 (%)
Weakness-Muscle weakness	15 (100.0)
Ptosis	7 (46.6)
Diplopia	2 (13.4)
Dysphagia	6 (40)
Respiratory Distress	4 (26.6)
Medical treatment in patients with Myasthenia Gravis	n=15 (%)
Anticholinesterase	7 (46.6)
Anticholinesterase + Steroid	5 (33.4)
Anticholinesterase + Steroid+ IVIG	2 (13.4)
Anticholinesterase + Steroid + Immunomodulator	1 (6.6)

ASA: American Society of Anesthesiologists scale, IVIG: Intravenous Immunoglobulin

After the procedure, all patients were taken to the ICU for at least 24 hours for close follow-up and treatment, especially in terms of postoperative residual block and respiratory complications. In the early postoperative period, complications such as reintubation due to respiratory failure, a decrease in peripheral O2 saturation below 90%, and PRNB were not observed Table 2.

Table 2. Peroperative period and postoperative complications

	MG+ Thymomas (n=15)	Thymomas (n=15)	p
Length of anesthesia (min.)	114.00±18.72	124.00±17.09	0.126
Length of surgery (min.)	98.67±18.36	106.00±16.38	0.258
Total dosage of rocuronium (mg/kg)	85.33±16.41	91.67±17.28	0.312
Total dosage of sugammadex (mg/kg)	166.67±36.18	176.67±31.99	0.429
The time from the start of spontaneous breathing to extubation (min.)	8.07±2.08	7.80±2.27	0.740
Time to maintain spontaneous breathing without aid (min.)	16.67±2.12	15.80±2.65	0.332
Hospital stay (day)	4.87±0.99	4.27±0.88	0.91
SpO2 lower than 90% within 24 hours	None	None	NA
Postoperative residual neuromuscular block	None	None	NA
Reintubations within 48 hours	None	None	NA

MG: Myasthenia Gravis

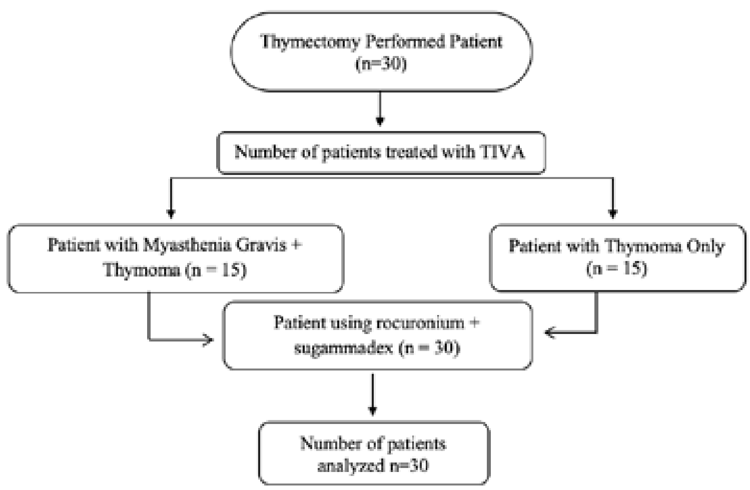

Figure 1. Flow chart of the study

Discussion

Thymectomy is a common surgical procedure in addition to pharmacological therapy for myasthenic patients. Major surgical approaches such as sternotomy and thoracotomy can be applied for thymectomy surgery. Both major surgery and the diagnosis of some patients with MG make the anesthesia-NMB approach and follow-up extremely important. Volatile agents reduce neuromuscular transmission [7]. Although it is known that the neuromuscular conduction returns in a short time after the inhaler general anesthesia are terminated, as an induction agent in thymectomy surgery in our clinic, we use propofol and fentanyl. We apply total intravenous anesthesia (TIVA) with propofol and remifentanil infusion for the maintenance of general anesthesia. Propofol can be safely preferred in patients with MG because it creates sufficient depth of anesthesia both as an induction agent and for the maintenance of anesthesia, provides rapid postoperative recovery, and causes less nausea and vomiting [8]. Remifentanil, an opioid analgesic, has features such as the rapid onset of action, low volume of distribution, rapid recovery even after prolonged use, the ability to provide a recovery profile without respiratory depression in the postoperative period, and metabolism by non-specific esterases. Because of these properties, remifentanil infusion can be preferred as a good analgesic in patients with MG [9,10]. In addition, the use of BIS monitoring in anesthesia depth monitoring eliminates the risk of superficial anesthesia as well as the negative effects of deep anesthesia. In thymectomy surgery, anesthesia depth is provided by TIVA titration with a BIS value between 40-60.

Regional anesthesia is a safe method for MG patients [11]. For thymectomy surgery, thoracic epidural analgesia (TEA) is very important in providing postoperative analgesia, hemodynamic stability, and rapid recovery. Chevalley et al. emphasized that the combination of TEA and TIVA in thymectomy operations provides optimal operation conditions, as well as being reliable and economical [12].

In our own clinic, we prefer to place a thoracic epidural catheter in our patients for both intraoperative and postoperative analgesia for thymectomy surgery. For this purpose, the thoracic epidural catheter was placed in 26 of our patients, while the procedure was unsuccessful in 4 patients. Bupivacaine, an amide local anesthetic, was preferred for epidural analgesia, intravenous opioids, paracetamol, or nonsteroidal analgesics were used in patients who could not insert a catheter or require additional analgesic.

Sternotomy was performed in 23 (76.7%) of our patients and thoracotomy in 7 (23.3%) of our patients during thymectomy surgery. In our patients, a single lumen endotracheal intubation tube was used in patients who underwent sternotomy, while a double-lumen intubation tube was used in patients who underwent thoracotomy. NMB is recommended for successful placement of the double-lumen tube, providing single-lung ventilation for surgical comfort and preventing spontaneous breathing efforts. Sungur et al. used a double-lumen tube in patients with myasthenia gravis who underwent video-assisted thoracoscopy and stated that muscle relaxation was necessary for patient comfort and hemodynamic stabilization [13]. The researchers used rocuronium at half the recommended dose for endotracheal intubation. In our own patient group, in terms of patient comfort and safe surgical procedure, a deep neuromuscular blockage was achieved by using rocuronium at a dose of 0.6 mg/kg, even if the patients were diagnosed with myasthenia gravis.

Sugammadex is a selective NMBA binding agent that reverses the effect of steroidal NMBAs (rocuronium and vecuronium). It neutralizes molecules by binding and reduces the amount of free NMBA molecules [14]. Initially, the use of sugammadex in myasthenia gravis patients was generally in the form of case reports. However, in the first large case series, generally reduced doses of rocuronium were applied, and in these series, sugammadex was used to eliminate the NMB effect. The investigators stated that NMB disappeared rapidly after sugammadex use and there were no postoperative complications [6,13].

Vymazal et al. used rocuronium at a dose of 0.6 mg/kg as NMBA in their large case series consisting of 117 myasthenia gravis cases undergoing surgical procedures. They used sugammadex at a dose of 4 mg/kg to antagonize NMB [3]. In our clinical practice, rocuronium was administered at a dose of 0.6 mg/kg, while sugammadex was administered at a dose of 2 mg/kg to antagonize the block. There was no difference in the total rocuronium and sugammadex dose used in thymoma cases with or without MG diagnosis. Similarly, when the time between the onset of spontaneous breathing and extubation in both patient groups and the time from the end of the surgery until the time the airway maneuver and ventilation not needed anymore were examined, there was no difference between the groups.

Postoperative residual neuromuscular block (PRNB) is still the most dangerous complication after general anesthesia using NMBAs. A recent study has shown that 26.7% of patients had PRNB after the use of non-depolarizing neuromuscular blockers [15]. PRNB did not occur in any of our patients. We think that this situation was caused by the use of sugammadex in all patients, being followed in the recovery unit in the operating room until the postoperative hemodynamic stability and normal muscle strength, and then being in the ICU for 24 hours.

Our study has some limitations. One of them is that there is no control group. Another is that the effect of sugammadex on steroid NMBA antagonism together with inhaler anesthesia in general anesthesia maintenance was not investigated. The effect of sugammadex at different doses (such as 8-16 mg/kg) and TOF values after different doses of sugammadex were not recorded.

While succinylcholine, a depolarizing NMB, is not recommended in MG patients, the use of non-depolarizing NMBA should be avoided. However, studies and case reports in recent years have shown that sugammadex safely reverses the effect of steroid non-depolarizing NMBAs in MG patients. This was confirmed in our study.

Conclusion

As a conclusion, we recommend using propofol as an IV general anesthetic agent in thymectomy surgery applied to patients with MG, performing TIVA using propofol and opioid analgesics in anesthesia maintenance, and providing a good peroperative analgesia control. In addition, sugammadex may be preferred for steroid NMBA antagonism in this patient group.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest
None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

References

1- Tormoehlen LM, Pascuzzi RM. Thymoma, myasthenia gravis, and other paraneoplastic syndromes. Hematol Oncol Clin North Am.2008;22(3):509-26. DOI: 10.1016/j.hoc.2008.03.004.
2- Bailey PD. Surgical approach to myasthenia gravis. In: Pearson's Thoracic and Esophageal Surgery. New York, NY: McGraw-Hill Companies, Inc; 2008. p.655–8.
3- Vymazal T, Krecmerova M, Bicek V, Lischke R. Feasibility of full and rapid neuromuscular blockade recovery with sugammadex in myasthenia gravis patients undergoing surgery - a series of 117 cases. Ther Clin Risk Manag. 2015;11:1593–6. DOI: 10.2147/TCRM.S93009.
4- Shah D, Dharmarajah A. Use of sugammadex in an octagenerian with myaesthenia gravis undergoing emergency laporotomy. J Clin Anesth. 2017;37:109–10. DOI: 10.1016/j.jclinane.2016.11.008.
5- Soyoral L, Goktas U, Cegin MB, Baydi V. Successful use of sugammadex for caesarean section in a patient with myasthenia gravis. Braz J Anesthesiol. 2017;67:221–2. DOI: 10.1016/j.bjane.2014.08.008.
6- De Boer HD, Shields MO, Booij LH. Reversal of neuromuscular blockade with sugammadex in patients with myasthenia gravis: a case series of 21 patients and review of the literature. Eur J Anaesthesiol. 2014;31 (12):715–21. DOI: 10.1097/EJA.0000000000000153.
7- Hirsch NP. Neuromuscular junction in health and disease. Br J Anaesth 2007; 99: 132-8. DOI: 10.1093/bja/aem144.
8- Sanjay OP, Prashanth P, Karpagam P, Tauro DI. Propofol or sevoflurane anesthesia without muscle relaxants for thymectomy in myasthenia gravis. Ind J Thoracic Cardiovas Surg 2004;20:83-7. DOI:10.1007/s12055-004-0047-2.
9- Mekis D, Kamenik M. Remifentanil and high thoracic epidural anaesthesia: a successful combination for patients with myasthenia gravis undergoing transsternal thymectomy. Eur J Anaesthesiol. 2005 May;22(5):397-9. DOI: 10.1017/s0265021505250676.
10- Ju-Mei Ng. Total intravenous anesthesia with propofol and remifentanil for video-assisted thoracoscopic thymectomy in patients with myasthenia gravis. Anesth Analg. 2006;103(1):256-7. DOI: 10.1213/01.ANE.0000215230.64071.A5.
11- Romero A, Joshi GP. Neuromuscular Disease and Anesthesia. Muscle Nerve 2013; 48;451-60. DOI: 10.1002/mus.23817.
12- Chevalley C, Spiliopoulos A, de Perrot M, Tschopp JM, Licker M. Perioperative medical management and outcome following thymectomy for myasthenia gravis. Can J Anaesth. 2001;48(5):446-51. DOI: 10.1007/BF03028306.
13- Sungur Ulke Z, Yavru A, Camci E, Ozkan B, Toker A, Senturk M. Rocuronium and sugammadex in patients with myasthenia gravis undergoing thymectomy. Acta Anaesthesiol Scand. 2013;57:745–8. DOI: 10.1111/aas.12123.
14- Blichfeldt-Lauridsen L, Hansen BD. Anesthesia and myasthenia gravis. Acta Anesthesiol Scand 2012; 56:17–22. DOI: 10.1111/j.1399-6576.2011.02558.x.
15- Errando CL, Garutti I, Mazzinari G, Diaz-Cambronero O, Bebawy JF, Grupo Espanol de Estudio del Bloqueo Neuromuscular. Residual neuromuscular blockade in the postanesthesia care unit. Observational cross-sectional study of a multicenter cohort. Minerva Anestesiologica 2016; 82: 1267–77.

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